

STATEMENT ON PROJECTED STUDY

to be submitted to

TOBACCO INDUSTRY RESEARCH COMMITTEE

By

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Experiments have been in process with "hallucinogenic" mushrooms administered to human subjects. Mixed effects have resulted and tentatively reported; (1), (2), (3). Separate investigations are being made to determine the clinical effects of an amino acid (L-tryptophane) and of vitamin B-complex. The probable correlation between the several experimental products is being studied primarily from the neuropsychopharmacological aspect. Some tentative correlations have been reported by one of us (see abstract of presentation at AIBS meeting, September 1959) where an emphasis upon niacin metabolism is made.

In the course of a mushroom experiment with one of us the subject (G. C.) and the other the observer (S.I.S.), where a rather prominent and uncomfortable parasympathetic (serotonin-like) stimulation seemed to occur (p. 48; b.p. 98/70; temp 97⁰, cold extremities), the smoking of a cigarette at this point of the situation immediately gave a favorable type of subjective relief with reading changes reaching to p. 58 and b.p. 108/65. Within a few minutes after the cigarette was smoked the readings returned to p. 48 and b.p. 104/70, and with the slowed down effect came the subjective comment, "I feel pretty miserable now". Another cigarette later in the test process produced less marked but comparable effects. In contrast to the cigarette, the stimulant, caffeine sodium benzote, when administered tended to reduce the pulse and blood pressure to lower levels p. 44 and b.p. 100/60 respectively.

Our intent is to determine the chemical substance in the mushroom which is causing the parasympathetic stimulation. It is evident that the cigarette smoking here contributed a desirable stimulatory effect and had offset the "slowed-down" physiology and feeling which occurred with the excessive parasympathetic stimulation.

It is our opinion that the nicotine of the cigarette was responsible for the enhancement of physiology and of feeling-tone observed here. Is this a more pronounced aspect of a mechanism or situation which obtains in the stimulatory effects arising generally in cigarette smoking? Is this a basic phase of the explanation for the latter? What relationship does nicotine have to niacin in the general stressor (Selye) or nervousness process? One of us (S.I.S.) contends that the sympathetic (with adrenalin-noradrenalin-histamine) part of the autonomic system produces the symptom-signs and feeling-tone of "nervousness" and the parasympathetic (acetylcholine) produces the symptom-signs and feeling tone of non-nervousness (slowed or quieting effect); whereas, the components of mood

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(euphoria versus depression) and associated energy are correlated with the status of the reticular (alerting) formation of the brain stem and is subserved by a phase of niacin metabolism.

In the further experimentation with the mushrooms or the chemical isolated from such and with L-tryptophane, the cigarette (nicotine) could be used as above in a further study of the observed effect as well as to determine the probable correlation with niacin metabolism. The further experimentation therefore should include laboratory examination of at least the niacin metabolites as they may be detected in the blood and the urine (Determined according to the methods used at the University of Wisconsin in their studies on L-tryptophane-niacin-serotonin (4).)

1. Observations On Agarics Causing Cerebral Mycetisms, Rolf Singer, Dr. S. I. Stein, Dr. Ralph W. Ames, and Dr. Alexander H. Smith. *Mycopathologia et Mycologia Applicata* - Vol. IX, 29-IX-1958, Fasc. 4.
2. Some Clinical and Chemical Observations Of *Panaeolus Venenosus*, *Panaeolus Sphinctrinus*, and *Psilocybe Caerulescens* Mushrooms. Sam I. Stein, M.D., Ph.D., *Mycologia*, Vol. L-1, January-February 1959.
3. Observations On Psychoneurophysiologically Significant Mushrooms. Sam I. Stein, Gerhard L. Closs and Norman W. Gabel. In press, *Mycopathologia et Mycologia Applicata*.
4. Disorders Of Tryptophane Metabolism. J. M. Price, University of Michigan Medical Bulletin, Vol. XXIV, pp. 461-485, 1958 (Dec.).

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ABSTRACT

Some Biochemical and Physiological Correlations Developed From Clinical Observations With Various Toxic Mushrooms and Medicinal Products.

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Clinical and some psychological measurements have been made after the ingestion of graduated amounts of *Panaeolus venenosus*, *Panaeolus sphinctrinus*, and *Psilocybe caerulescens* mushrooms. These are compared with observations derived in clinical practice resulting from the application of psychopharmacological products (reserpine, iproniazid, vitamins, and some amino acids). Some practical correlations appear permissible at this time. Recurring effects and some variations will be presented. The latter might be explained on the basis of individual biochemical differences.

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The full paper is to be published in the Proceedings of the Society of Industrial Microbiology, 1959.

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